OIPE
MAR 18 2009
PATENT & TRADEMARK OFFICE
MAP91

SEQUENCE LISTING

<110> Berislav V. ZLOKOVIC
John H. GRIFFIN

<120> NEUROPROTECTIVE ACTIVITY OF ACTIVATED PROTEIN C INDEPENDENT OF ITS ANTICOAGULANT ACTIVITY

<130> 5192-16

<140> US 10/537,545
<141> 2006-12-18

<150> PCT/US2003/038764
<151> 2003-12-05

<150> US 60/465,235
<151> 2003-04-25

<150> US 60/442,066
<151> 2003-01-24

<150> US 60/439,936
<151> 2002-12-05

<160> 1

<170> MS Word

<210> 1
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> peptide

<400> 1
Thr Phe Leu Leu Arg Asn Pro Asn Asp Lys
1 5 10

-continued

ACA	GCG	GCC	CAC	TGC	ATG	GAT	GAG	TCC	AAG	AAG	CTC	CTT	GTC
AGG	CTT	GGA	GAG	TAT	GAC	CTG	CGG	CGC	TGG	GAG	AAG	TGG	GAG
CTG	GAC	CTG	GAC	ATC	AAG	GAG	GTC	TTC	GTC	CAC	CCC	AAC	TAC
AGC	AAG	AGC	ACC	ACC	GAC	AAT	GAC	ATC	GCA	CTG	CTG	CAC	CTG
GCC	CAG	CCC	GCC	ACC	CTC	TCG	CAG	ACC	ATA	GTG	CCC	ATC	TGC
CTC	CCG	GAC	AGC	GGC	CTT	GCA	GAG	CGC	GAG	CTC	AAT	CAG	GCC
GGC	CAG	GAG	ACC	CTC	GTG	ACG	GGC	TGG	GGC	TAC	CAC	AGC	AGC
CGA	GAG	AAG	GAG	GCC	AAG	AGA	AAC	CGC	ACC	TTC	GTC	CTC	AAC
TTC	ATC	AAG	ATT	CCC	GTG	GTC	CCG	CAC	AAT	GAG	TGC	AGC	GAG
GTC	ATG	AGC	AAC	ATG	GTG	TCT	GAG	AAC	ATG	CTG	TGT	GCG	GGC
ATC	CTC	GGG	GAC	CGG	CAG	GAT	GCC	TGC	GAG	GGC	GAC	AGT	GGG
GGG	CCC	ATG	GTC	GCC	TCC	TTC	CAC	GGC	ACC	TGG	TTC	CTG	GTG
GGC	CTG	GTG	AGC	TGG	GGT	GAG	GGC	TGT	GGG	CTC	CTT	CAC	AAC
TAC	GGC	GTT	TAC	ACC	AAA	GTC	AGC	CGC	TAC	CTC	GAC	TGG	ATC
CAT	GGG	CAC	ATC	AGA	GAC	AAG	GAA	GCC	CCC	CAG	AAG	AGC	TGG
GCA	CCT	TAG—3'											

wherein
A is deoxyadenyl,
G is deoxyguanyl,

R is 5'-GCC CAC CAG GTG CTG CGG ATC CGC AAA CGT-3',
R^1 must necessarily be

5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT—3';

C is deoxycytidyl,
T is thymidyl,
R is 5'-GCC CAC CAG GTG CTG CGG ATC CGC, AAA CGT-3' or 5'-CAC CAG GTG CTG

and that when
R is 5'-CAC CAG GTG CTG CGG ATC CGC AAA CGT-3',
R^1 must necessarily be

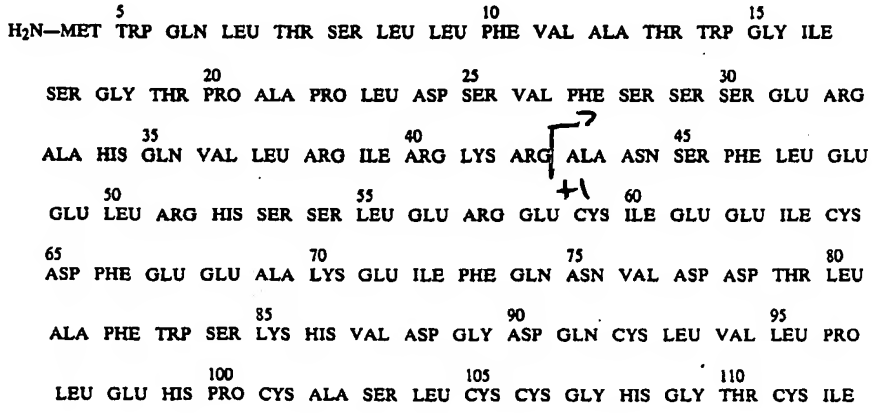
5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT GCC—3'.

CGG ATC CGC AAA CGT-3'
R^1 is

5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT—3'
or 5'-ATG	TGG	CAG	CTC	ACA	AGC	CTC	CTG	CTG	TTC GTG
GCC	ACC	TGG	GGA	ATT	TCC	GGC	ACA	CCA	GCT CCT
CTT	GAC	TCA	GTG	TTC	TCC	AGC	AGC	GAG	CGT GCC—3'

M is 0 or 1, and
N is 0 or 1,
provided that when M is 0, N must necessarily also be 0; and that when

The compounds of the present invention encode human protein C, and the heretofore unknown amino acid sequence of nascent human protein C when M and N are 1. The amino acid sequence, numbered to facilitate further discussion, of nascent human protein C is:



-continued

```
                115                 120                 125
ASP GLY ILE GLY SER PHE SER CYS ASP CYS ARG SER GLY TRP GLU GLY

    130                 135                 140
ARG PHE CYS GLN ARG GLU VAL SER PHE LEU ASN CYS SER LEU ASP ASN

145                 150                 155                 160
GLY GLY CYS THR HIS TYR CYS LEU GLU GLU VAL GLY TRP ARG ARG CYS

            165                 185                 190
SER CYS ALA PRO GLY TYR LYS LEU GLY ASP ASP LEU LEU GLN CYS HIS

        180                 185                 190
PRO ALA VAL LYS PHE PRO CYS GLY ARG PRO TRP LYS ARG MET GLU LYS

    195                 200                 205
LYS ARG SER HIS LEU LYS ARG ASP THR GLU ASP GLN GLU ASP GLN VAL

    210                 215                 220
ASP PRO ARG LEU ILE ASP GLY LYS MET THR ARG ARG GLY ASP SER PRO

225                 230                 235                 240
TRP GLN VAL VAL LEU LEU ASP SER LYS LYS LYS LEU ALA CYS GLY ALA

            245                 250                 255
VAL LEU ILE HIS PRO SER TRP VAL LEU THR ALA ALA HIS CYS MET ASP

        260                 265                 270
GLU SER LYS LYS LEU LEU VAL SRG LEU GLY GLU TYR ASP LEU ARG ARG

    275                 280                 285
TRP GLU LYS TRP GLU LEU ASP LEU ASP ILE LYS GLU VAL PHE VAL HIS

    290                 295                 300
PRO ASN TYR SER LYS SER THR THR ASP ASN ASP ILE ALA LEU LEU HIS

305                 310                 315                 320
LEU ALA GLN PRO ALA THR LEU SER GLN THR ILE VAL PRO ILE CYS LEU

            325                 330                 335
PRO ASP SER GLY LEU ALA GLU ARG GLU LEU ASN GLN ALA GLY GLN GLU

        340                 345                 350
THR LEU VAL THR GLY TRP GLY TYR HIS SER SER ARG GLU LYS GLU ALA

    355                 360                 365
LYS ARG ASN ARG THR PHE VAL LEU ASN PHE ILE LYS ILE PRO VAL VAL

    370                 375                 380
PRO HIS ASN GLU CYS SER GLU VAL MET SER ASN MET VAL SER GLU ASN

385                 390                 395                 400
MET LEU CYS ALA GLY ILE LEU GLY ASP ARG GLN ASP ALA CYS GLU GLY

            405                 410                 415
ASP SER GLY GLY PRO MET VAL ALA SER PHE HIS GLY THR TRP PHE LEU

        420                 425                 430
VAL GLY LEU VAL SER TRP GLY GLU GLY CYS GLY LEU LEU HIS ASN TYR

    435                 440                 445
GLY VAL TYR THR LYS VAL SER ARG TYR LEU ASP TRP ILE HIS GLY HIS

        450                 455                 460
ILE ARG ASP LYS GLU ALA PRO GLN LYS SER TRP ALA PRO—COOH
```

wherein
H_2N- is the amino-terminus,
—COOH is the carboxy-terminus,
ALA is Alanine,
ARG is Arginine,
ASN is Asparagine,
ASP is Aspartic acid,
CYS is Cysteine,
GLN is Glutamine,
GLU is Glutamic Acid,
GLY is Glycine,
HIS is Histidine,
ILE is Isoleucine,
LEU is Leucine,
LYS is Lysine,
MET is Methionine,
PHE is Phenylalanine,
PRO is Proline,
SER is Serine,
THR is Threonine,
TRP is Tryptophan,
TYR is Tyrosine, and
VAL is Valine.

The DNA compounds of the present invention are derived from cDNA clones prepared from human liver mRNA that encodes human protein C activity. In con-